UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/622,293	07/17/2003	Toby Freyman	10177-118-999	5795

7590 08/19/2008

John A. Bauer
C/O Fulbright & Jaworski L.L.P.
666 Fifth Avenue
New York, NY 10103-3198

EXAMINER	
NGUYEN, QUANG	

ART UNIT	PAPER NUMBER
1633	

MAIL DATE	DELIVERY MODE
08/19/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/622,293	FREYMAN ET AL.	
	Examiner	Art Unit	
	QUANG NGUYEN, Ph.D.	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *13 May 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,5-27,30-35 and 42* is/are pending in the application.

4a) Of the above claim(s) *16-26,31-34 and 42* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,5-15,27,30 and 35* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5/15/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's amendment filed on 5/13/08 was entered.

Amended claims 1, 5-27, 30-35 and new claim 42 are pending in the present application.

Applicants elected previously Group I, drawn to a method for producing a decellularized extracellular matrix material containing a biological material or for producing a tissue regeneration scaffold for implantation into a patient wherein the step of conditioning a body tissue of a donor animal by genetic engineering and allowing the conditioned body tissue to produce the biological material are conducted prior to harvesting the conditioned body tissue from the donor animal. Applicants further elected the following species with traverse in the reply filed on 9/19/05, (a) bone marrow as a species of a body tissue; (b) VEGF as a species of a biological material; and (c) human as a species of a donor animal.

This application contains claims 16-26 and 31-34 drawn to an invention nonelected without traverse in the reply filed on 9/19/05. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

New claim 42 is withdrawn from further consideration because it is directed to a non-elected species.

Accordingly, amended claims 1, 5-15, 27, 30 and 35 are examined on the merits herein with the aforementioned elected species.

Response to Amendment

The rejection under 35 U.S.C. 102(b) as being anticipated by Vituri et al. (Brazilian Journal of Medical and Biological Research 33:889-895, 2000) was withdrawn in light of Applicant's amendment.

The rejection under 35 U.S.C. 102(e) as being anticipated by Mitchell et al (US 2002/0115208) was withdrawn in light of Applicant's amendment.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 5, 8-15, 27 and 35 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naughton (US 5,830,708; IDS) in view of Mitchell et al (US 2002/0115208), Patel et al. (US 7,087,089) and Wolff et al. (WO 99/55379; IDS) for the same reasons already set forth in the Office action mailed on 11/14/2007 (pages 6-10). ***The same rejection is restated below.***

With respect to the elected species, Naughton teaches a method for producing a composition containing naturally secreted human extracellular matrix material, said method comprises the steps of: (a) culturing extracellular matrix secreting human stromal cells from tissues/organs obtained by appropriate biopsy or upon autopsy, including aspirated bone marrow from normal human adult volunteers (col. 5, lines 48-

54; col. 15, lines 7-9), on a biocompatible three dimensional framework *in vitro*; (b) the stromal cells are killed after secretion of the extracellular matrix onto the framework and the cells and cellular contents are removed from the framework (col. 11, line 62 continues to line 63 of col. 12); (c) the extracellular matrix material deposited on the framework is collected and further processed to obtain a physiologically acceptable composition (col. 12, line 66 continues to line 20 of col. 14). Naughton further teaches that it may be desirable to prepare an extracellular matrix containing a foreign gene product, growth factor, regulatory factor and in such a situation the cells are genetically engineered to express the gene product that is immobilized in the extracellular matrix laid down by the stromal cells (col. 10, line 59 continues to line 22 of col. 11). This is a conditioning step. Naughton teaches that preferably, the expression control elements used should allow for the regulated expression of the gene so that the product can be over-synthesized in culture (col. 11, lines 15-17). Furthermore, Naughton teaches that biologically active substances such as proteins and drugs can also be incorporated in the composition for release or controlled release of these active substances after injection of the composition that include tissue growth factors such as TGF-beta and the like which promote healing and tissue repair at the site of injection (col. 13, lines 12-22). Naughton teaches that the extracellular matrix preparation is capable of promoting connective tissue deposition, angiogenesis, reepithilialization and fibroplasias, which is useful in the repair of skin and other tissue defects, and that the preparation is used to repair tissue defects by injection at the site of the defect (col. 3, lines 43-48; col. 13, line 43 continues to line 20 of col. 14). It should be noted that the term “body tissue” is

defined by the instant specification broadly encompasses any or a number of cells, tissues or organs (see page 7, lines 7-8).

Naughton does not specifically teach a method for producing a decellularized extracellular matrix containing a biological material, comprising the step of conditioning (genetic engineering is the elected invention) a body tissue (bone marrow is the elected species) of a donor animal (human is the elected species) to produce the biological material **prior to the step of harvesting the conditioned body tissue from the donor animal and decellularizing the conditioned body tissue**.

However, at the effective filing date of the present application Mitchell et al also disclosed methods for producing decellularized tissue engineered constructs and decellularized engineered native tissues for implanting into an individual in need thereof (see at least the abstract; Summary of the Invention), and taught that although in general production of the tissue engineered construct involves culturing the developing tissue primarily *in vitro*, **tissue engineered constructs produced at least in part by culturing the tissue *in vivo* are also contemplated** (page 5, bottom of paragraph 67). Mitchell et al further taught that there is a need to **expose developing tissue engineered constructs to certain stimuli, so that the resulting construct develops properties and structure that more closely resemble those of the corresponding naturally occurring tissue** (paragraph 96).

Patel et al also taught a process for preparing acellular extracellular matrix materials useful for supporting cell growth *in vivo* and *in vitro* (see at least Summary of the Invention). Patel et al further disclosed that **the acellular collagen-containing**

extracellular matrices can be derived from renal capsular tissues harvested from either transgenic animals (pre-conditioned donor animal) or non-transgenic animals, and that animals encompass mammals, preferably porcine, bovine or ovine (col. 3, lines 11-21).

Wolff et al also disclosed **a process for delivering a polynucleotide encoding a protein of interest (e.g., hormones, cytokines, growth factors and others) into parenchymal cells within tissues *in situ* and *in vivo*, including parenchymal cells of bone marrow within a mammal** (see at least Summary of the Invention; and page 8, second paragraph; page 7, first paragraph).

Accordingly, it would have been obvious for an ordinary skilled artisan in the art to modify the method of Naughton by also preparing a decellularized bone marrow extracellular matrix material harvested from the bone marrow of a donor animal, including a human donor, whose parenchymal cells of the bone marrow have been transfected with a polynucleotide encoding a protein of interest in light of the teachings of Mitchell et al., Patel et al. and Wolff et al. as discussed above.

An ordinary skilled artisan would have been motivated to carry out the above modification because acellular extracellular matrix materials useful for supporting cell growth *in vivo* and *in vitro* has been taught by Patel et al can be harvested from a transgenic animal. Additionally, Mitchell et al also taught the preparation of decellularized tissue engineered constructs and/or decellularized engineered native tissues, wherein the tissue engineered constructs can be produced at least in part by culturing the tissue *in vivo*. Moreover, unlike the decellularized extracellular matrix

prepared *in vitro* or in cultured conditions, the conditioned bone marrow extracellular matrix to be harvested from a donor animal has been subjected to the same physiological conditions as a naturally occurring bone marrow. Furthermore, Wolff et al already disclosed successfully a process for delivering a polynucleotide encoding any protein of interest in parenchymal cells of bone marrow within a mammal.

An ordinary skilled artisan would have a reasonable expectation of success to carry out the above modification in light of the teachings of Naughton, Mitchell et al., Patel et al., and Wolff et al., coupled with a high level of skills of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Response to Arguments

Applicants' arguments with respect to the above rejection in the Amendment filed on 5/13/08 (pages 11-14) have been fully considered but they are respectfully not found persuasive for the reasons discussed below.

1. Applicants argue that the Examiner used hindsight reconstruction to pick and choose among isolated disclosures in the prior art to arrive at the presently claimed invention. Applicants further argue that an ordinary skill in the art would have no reason to combine the teachings of Naughton with anyone of Mitchell et al., Patel et al. and Wolff et al since the references each employs different body tissues and/or different techniques to achieve different objectives. Particularly, a person of ordinary skill in the

art would have no reason to substitute the genetic conditioning step in Naughton with the physical conditioning step (e.g., mechanical or electrical stimuli) in Mitchell et al since different conditioning steps require different materials and would have different effects on the cells, and without guidance a combination or substitution of conditioning steps from these references would lead to unpredictable results. Applicants also argue that the conditioning step in Naughton differs from that of Patel et al since Naughton discloses conditioning cells on a framework outside of the body (e.g., in vitro or ex vivo) while Patel et al suggest the use of transgenic animal as a source of conditioned cells. Transgenic animals are produced in vivo or in situ, and cannot be separately grown on a three-dimensional framework; and therefore one of ordinary skill in the art would have no reason to use the transgenic animal of Patel et al in the conditioning step of Naughton. Applicants further argue that Naughton and Wolff et al each uses different materials in their respective conditioning step. While the method of Naughton conditions human stromal cells that comprises fibroblasts derived from adult or fetal tissue (col. 7, lines 64-66), Wolff et al explicitly state that parenchymal cells are different from cells of the connective and exclude fibroblasts (page 7, lines 16-20); and therefore teach away from the stromal cells of Naughton. Based on the teachings of Wolff et al, a person of ordinary skill in the art would reasonably expect stromal cells and parenchymal cells to be structurally and functionally different and each would require a different approach for conditioning and culturing. Thus, the person of ordinary skill in the art would have no reason to apply the delivery process of Wolff et al to the stromal cells used in the methods of Naughton.

Firstly, It must be recognized that any judgment on obviousness is in a sense necessarily a reconstruction based upon hindsight reasoning. But so long as it takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made, and does not include knowledge gleaned only from the applicant's disclosure, such a reconstruction is proper. See *In re McLaughlin*, 443 F.2d 1392, 170 USPQ 209 (CCPA 1971).

Secondly, it is noted that Applicants did not take into consideration the totality of the teachings of Naughton, Mitchell et al, Patel et al and Wolff et al. It appears that Applicants only consider the teachings of Naughton alone, Naughton together with Mitchell et al or with Patel et al or with Wolff et al in isolations.

Thirdly, please note that the above rejection is under 35 U.S.C. 103(a), and therefore none of the cited references has to teach every limitation of the instant claims, particularly with respect to the elected species.

Fourthly, the citation of the teachings of Mitchell et al **is not about a substitution of the genetic conditioning step in Naughton with the physical conditioning step (e.g., mechanical or electrical stimuli)** in Mitchell et al as argued by Applicants. As noted in the above rejection, Mitchell et al taught clearly that although in general production of the tissue engineered construct involves culturing the developing tissue primarily *in vitro*, **tissue engineered constructs produced at least in part by culturing the tissue *in vivo* are also contemplated** (page 5, bottom of paragraph 67). Mitchell et al further taught that there is a need to **expose developing tissue engineered constructs to certain stimuli, so that the resulting construct**

develops properties and structure that more closely resemble those of the corresponding naturally occurring tissue (paragraph 96). Additionally, stimuli that are taught by Mitchell et all are not necessarily limited only mechanical or electrical stimuli, but they also include **chemical stimuli and others to produce a tissue engineered construct having desirable mechanical, physical or biochemical properties** (see at least paragraphs 67 and 76-77). Accordingly, unlike the decellularized extracellular matrix prepared *in vitro* or in cultured conditions taught by Naughton, **the genetic engineering conditioned bone marrow extracellular matrix to be harvested from a donor animal resulting from the modified teachings has been subjected to the same physiological conditions as a naturally occurring bone marrow; and therefore it has more desirable properties and/or structures** as clearly contemplated and suggested by Mitchell et al. Once again, Mitchell et al taught explicitly that **tissue engineered constructs produced at least in part by culturing the tissue in vivo**.

Fifthly, the citation of the teachings of Patel et al **is also not about growing transgenic animals on a three-dimensional framework as argued by Applicants**. The teachings of Patel et al demonstrated clearly that at the filing date of the present application, **the concept of preparing acellular collagen-based extracellular matrices derived from an organ harvested from both non-transgenic and transgenic animals (genetically conditioning donor animals) to be used as a tissue graft and/or cell growth material was already taught**.

Sixthly, there is no "teaching away" whatsoever by the Wolff et al reference with respect to the primary Naughton reference. Naughton stated clearly "**[s]tromal cells of hematopoietic tissue including, but not limited to, fibroblast endothelial cells, macrophages/monocytes, adipocytes and reticular cells, can be used to form the three-dimensional subconfluent stroma for the production of a bone marrow specific extracellular matrix in vitro, see infra**" (col. 9, lines12-17). Additionally, Naughton **taught clearly culturing extracellular matrix secreting human stromal cells from tissues/organs obtained by appropriate biopsy or upon autopsy, including aspirated bone marrow from normal human adult volunteers** (col. 5, lines 48-54; col. 15, lines 7-9). Wolff et al stated "Parenchymal cells are the distinguishing cells of a gland or organ contained in and supported by the connective tissue framework. The parachymal cells typically perform a function that is unique to the particular organ. The term "parenchymal" **often excludes** cells that are common to many organs and tissues such as fibroblasts and endothelial cells within the blood vessels" (page 7, lines 17-21). **This paragraph simply distinguishes parenchymal cells and cells that are common to many organs and tissues**. Furthermore, Wolff et al stated "In spleen, thymus, lymph nodes and **bone marrow, the parenchymal cells include recitular cells and blood cells (or precursors to blood cells) such as lymphocytes, monocytes, plasma cells and macrophages**" (page 8, lines 4-6). The Wolff et al reference showed clearly that **at the filing date of the present application, an ordinary skilled artisan could deliver successfully a polynucleotide encoding any protein of interest in parenchymal cells of bone marrow within a mammal**.

Therefore, **an ordinary skilled artisan would have a reasonable expectation of success** to carry out the modifications as set forth above in light of the teachings of Naughton, Mitchell et al., Patel et al., and Wolff et al., coupled with a high level of skills of an ordinary skilled artisan in the relevant art.

2. Applicants argues that the teachings of Naughton is complete for its intended purpose and thus a person of ordinary skill in the art would have no motivation to use any additional references, let alone three secondary references to modify the teachings of Naughton. Similar to the Lubowe patent in *In re Herschler*, the solution taught by Naughton is complete, and therefore it provides no reason to look to the art for alternative steps to condition the cells and in particular no motivation to look to the transgeneic animal of Patel et al, the physical conditioning of Mitchell et al., and the polynucleotide delivery system of Wolf et al. Applicants further argue that the conditioning step in Mitchell et al. must occur **after** the body tissue is harvested; Patel et al do not teach or suggest that a body tissue of a transgenic animal is the tissue which is harvested and decellularized as required by the claimed methods; and Wolff et al do not teach or suggest harvesting the parenchymal cells. Accordingly, none of Mitchell et al, Patel et al and Wolff et al cures the deficiency of Naughton.

Once again, it appears that Applicants only consider the teachings of Naughton alone, Naughton together with Mitchell et al or with Patel et al or with Wolff et al in isolations. **The teachings of Mitchell et al, Patel et al and Wolf et al provide clearly motivations and/or suggestions for an ordinary skilled artisan to improve the**

teachings and/or the production of an improved human decellularized bone marrow specific extracellular matrix for the repair of at least soft tissue and skin defects. Please refer to the above rejection and Examiner's responses in the preceding paragraphs.

Claims 13 (VEGF embodiment) and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naughton (US 5,830,708; IDS) in view of Mitchell et al (US 2002/0115208), Patel et al. (US 7,087,089) and Wolff et al. (WO 99/55379; IDS) as applied to claims 1, 5, 8-15 and 27 above, and further in view of Herlyn et al. (WO 98/39035; Cited previously) for the same reasons already set forth in the Office action mailed on 11/14/2007 (pages 11-12). ***The same rejection is restated below.***

The combined teachings of Naughton, Mitchell et al., Patel et al. and Wolff et al. were presented above. However, none of the references teaches specifically that bone marrow is transfected with a nucleic acid encoding VEGF.

However, at the effective filing date of the present application Herlyn et al already teach growth factors, particularly VEGF is useful in wound repair in mammalian tissue by enhancing fibroblast growth and formation into a matrix, enhancing keratinocyte growth and angiogenesis and *ex vivo* method for infecting tissue to be transplanted with a recombinant virus expressing VEGF prior to transplantation (at least page 6, lines 14-23).

Accordingly, it would have been obvious for an ordinary skilled artisan in the art to further modify the combined method of Naughton, Mitchell et al., Patel et al. and

Wolff et al. by also selecting VEGF as an foreign gene product to be incorporated into the decellularized extracellular matrix in light of the teachings of Herlyn et al.

An ordinary skilled artisan would have been motivated to carry out the above modification because Herlyn et al already teach growth factors, particularly VEGF is useful in wound repair in mammalian tissue by enhancing fibroblast growth and formation into a matrix, enhancing keratinocyte growth and angiogenesis, and that this would enhance the clinical value for the composition containing the decellularized extracellular matrix material resulting from the combined teachings of Naughton, Mitchell et al., Patel et al. and Wolff et al.

An ordinary skilled artisan would have a reasonable expectation of success to carry out the above modification in light of the teachings of Naughton, Mitchell et al., Patel et al. Wolff et al., and Herlyn et al., coupled with a high level of skills of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 6-7 are rejected under 35 U.S.C. 103(a) as being unpatentable over Naughton (US 5,830,708; IDS) in view of Mitchell et al (US 2002/0115208), Patel et al. (US 7,087,089) and Wolff et al. (WO 99/55379) as applied to claims 1, 5, 8-15 and 27 above, and further in view of Schwarz et al. (US 6,656,916) for the same reasons already set forth in the Office action mailed on 11/14/2007 (pages 12-14). ***The same rejection is restated below.***

The combined teachings of Naughton, Mitchell et al., Patel et al. and Wolff et al. were presented above. However, none of the references teaches specifically that a further step of delivering a therapeutic agent to the body tissue before or after the conditioning step.

However, at the effective filing date of the present application, Schwartz et al already taught **a method of increasing the cellular expression of a gene in a biological tissue in an animal, including a bone marrow in a human**, said method comprises administering to said animal a pharmacologically effective dose of a glucocorticoid in an amount sufficient to increase the cellular expression of said gene (see at least col. 2, lines 35-51; col. 5, lines 54-59). Schwartz et al taught specifically that any glucocorticoid such as hydrocortisone, prednisone, prednisolone, triamcinolone, betamethasone, budesonide, flunisolide and dexamethasone can be used (col. 5, lines 31-37). The glucocorticoid may be administered concurrently with the delivery of the gene, **prior to the delivery of the gene or after delivery of the gene** (col. 5, lines 48-51).

Accordingly, it would have been obvious for an ordinary skilled artisan in the art to further modify the combined method of Naughton, Mitchell et al., Patel et al. and Wolff et al. by also administering to the donor animal a therapeutic agent such as a glucocoritoid to a body tissue prior to or after the gene delivery in light of the teachings of Schwarz et al.

An ordinary skilled artisan would have been motivated to carry out the above modification because the administration of a therapeutic agent such as a glucocorticoid

prior to or after the delivery of a gene would enhance the cellular expression of a delivered gene in a biological tissue, including a bone marrow in a human, as taught by Schwartz et al.

An ordinary skilled artisan would have a reasonable expectation of success to carry out the above modification in light of the teachings of Naughton, Mitchell et al., Patel et al. Wolff et al., and Schwarz et al., coupled with a high level of skills of an ordinary skilled artisan in the relevant art.

Therefore, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Response to Arguments

Applicants' arguments with respect to the above rejections further in view of either Herlyn et al. or Schwarz et al. in the Amendment filed on 5/13/08 (page 14) have been fully considered but they are respectfully not found persuasive for the reasons discussed below.

Applicants argue basically that neither Herlyn et al nor Schwarz et al cure the deficiencies of Naughton and their teachings are taken out of context and improperly combined with the remaining references.

With respect to the deficiencies of Naughton, please refer to the Examiner's responses to Applicant's arguments for the rejection of claims 1, 5, 8-15 and 27 above. Additionally, please refer to the motivations already set forth in the above rejections why an ordinary skilled artisan would be motivated to further modify the combined teachings

of Naughton, Mitchell et al, Patel et al and Wolff et al in light of the teachings of either Herlyn et al or Schwarz et al.

Conclusion

No claim is allowed.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Quang Nguyen, Ph.D., whose telephone number is (571) 272-0776.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's SPE, Joseph T. Woitach, Ph.D., may be reached at (571) 272-0739.

To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Group Art Unit 1633; Central Fax No. (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance.

Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your application serial or patent number, the type of document you are having an image problem with, the number of pages and the specific nature of the problem. The Patent Electronic Business Center will notify applicants of the resolution of the problem within 5-7 business days. Applicants can also check PAIR to confirm that the problem has been corrected. The USPTO's Patent Electronic Business Center is a complete service center supporting all patent business on the Internet. The USPTO's PAIR system provides Internet-based access to patent application status and history information. It also enables applicants to view the scanned images of their own application file folder(s) as well as general patent information available to the public.

/QUANG NGUYEN, Ph.D./

Primary Examiner, Art Unit 1633